

## **Supplementary file for**

### **Involvement of Cardiovascular System As The Critical Point in Coronavirus Disease 2019 (COVID-19) Prognosis and Recovery**

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**Appendix. Definitions of the terms used in table 1, table 2, table 3 and table 4.**

**Comments about the status of each cohort at the time of the study.**

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<b>Guan<sup>1</sup></b>	<p><b>Severe cases:</b> Definitions of “severe” to “non-severe” were evaluated at the time of admission using the American Thoracic Society guidelines for community-acquired pneumonia<sup>2</sup>.</p> <p><b>Recovery:</b> No definition.</p> <p><b>Cardiovascular Disease:</b> Patients with coronary heart disease..</p> <p><b>Comments:</b> 1029/1099 (93.6) patients remained hospitalized at the time of the study.</p>
<b>Huang<sup>3</sup></b>	<p><b>Severe cases:</b> Admission to an ICU. No further definition or criteria for ICU admission.</p> <p><b>Recovery:</b> Fitness for discharge was based on abatement of fever for at least 10 days, with improvement of chest radiographic evidence and viral clearance in respiratory samples from upper respiratory tract.</p> <p><b>Cardiovascular Disease:</b> No definition.</p> <p><b>Myocardial Injury:</b> Blood levels of hypersensitive troponin I above the 99th percentile upper reference limit (&gt;28 pg/mL) or new abnormalities shown on electrocardiography and echocardiography.</p> <p><b>Comments:</b> 7/41 (17.1) patients remained hospitalized at the time of the study.</p>

<b>Wang et al<sup>4</sup></b>	<p><b>Severe cases:</b> Admission to an ICU. No further definition or criteria for ICU admission.</p> <p><b>Recovery:</b> No definition.</p> <p><b>Cardiovascular Disease:</b> No definition.</p> <p><b>Myocardial Injury:</b> Cardiac injury was defined if the serum levels of cardiac biomarkers (eg, troponin I) were above the 99th percentile upper reference limit or new abnormalities were shown in electrocardiography and echocardiography.</p> <p><b>Arrhythmia:</b> No definition.</p> <p><b>Comments:</b> 17/138 (12.3) patients remained hospitalized at the time of the study.</p>
<b>Zhang et al<sup>5</sup></b>	<p><b>Severe cases:</b> Severe COVID-19 was designated when the patients had one of the following criteria: (a) respiratory distress with respiratory frequency <math>\geq 30/\text{min}</math>; (b) pulse oximeter oxygen saturation <math>\leq 93\%</math> at rest; and (c) oxygenation index (artery partial pressure of oxygen/inspired oxygen fraction, <math>\text{PaO}_2/\text{FiO}_2</math>) <math>\leq 300</math> mmHg.</p> <p><b>Cardiovascular Disease:</b> No definition.</p> <p><b>Comments:</b> 3/140 (2.1) patients were hospital staff and they all had non-severe COVID-19.</p>
<b>Wu et al<sup>6</sup></b>	<p><b>Severe cases:</b> Patients who developed acute respiratory distress syndrome (ARDS). ARDS was defined according to the World Health Organization (WHO) interim guidance<sup>7</sup>.</p> <p><b>Recovery:</b> No definition.</p> <p><b>Cardiovascular Disease:</b> No definition.</p> <p><b>Myocardial Injury:</b> Patients with CK-MB <math>&gt; 24\text{U/L}</math>.</p> <p><b>Comments:</b> 13/201 (6.5) patients remained hospitalized at the time of the study.</p>

- Guan et al<sup>8</sup>**      **Severe cases:** Patients were classified as having severe or non-severe Covid-19 based on the 2007 American Thoracic Society / Infectious Disease Society of America guidelines<sup>2</sup>.
- Cardiovascular Disease:** No definition.
- Comments:** Data analysis from 1590 laboratory-confirmed hospitalized patients in 575 hospitals of 31 province/autonomous regions/provincial municipalities across mainland China.
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- Yang et al<sup>9</sup>**      **Severe cases:** Critically ill patients. Critically ill patients were defined as those admitted to the intensive care unit (ICU) who required mechanical ventilation or had a fraction of inspired oxygen (FiO<sub>2</sub>) of at least 60% or more.
- Recovery:** No definition.
- Cardiovascular Disease:** Patients with coronary heart disease.
- Myocardial Injury:** Serum concentration of hypersensitive cardiac troponin I (hsTNI) above the upper limit of the reference range (>28 pg/mL), measured in the laboratory of Jin Yin-tan Hospital.
- Comments:** Of the 20/52 critically ill patients who survived, eight patients were discharged. Three patients were still on invasive ventilation at 28 days, including one patient who was also on ECMO. One patient was on non-invasive ventilation, two were using high-flow nasal cannula, and six were using common nasal cannula.

<b>Huang et al<sup>10</sup></b>	<p><b>Severe cases:</b> Patients were grouped into severe and non-severe COVID-19 according to the Chinese National Health Commission guidelines (Trial Version 5)<sup>11</sup>.</p> <p><b>Recovery:</b> The criteria for discharge were based on the guidelines for the diagnosis and treatment of novel coronavirus infection by the Chinese National Health Commission (Trial Version 5)<sup>11</sup>.</p> <p><b>Cardiovascular Disease:</b> No definition.</p> <p><b>Myocardial Injury:</b> Patients with cardiac troponin I (cTnI) above the 99th percentile upper reference limit.</p> <p><b>Comments:</b> 183/221 (82.8) patients remained hospitalized at the time of the study.</p>
<b>Xu et al<sup>12</sup></b>	<p><b>Cardiovascular Disease:</b> No definition.</p> <p><b>Comments:</b> It is a retrospective, single-center cohort study, in which all included patients had been discharged or had died.</p>
<b>Zhou et al<sup>13</sup></b>	<p><b>Recovery:</b> The criteria for discharge were: absence of fever for at least 3 days, substantial improvement in both lungs in chest CT, clinical remission of respiratory symptoms and two throat-swab samples negative for SARS-CoV-2 RNA obtained at least 24 h apart.</p> <p><b>Cardiovascular Disease:</b> Patients with coronary heart disease.</p> <p><b>Myocardial Injury:</b> Patients with serum levels of cardiac biomarkers (eg, high-sensitivity cardiac troponin I) above the 99<sup>th</sup> percentile upper reference limit, or new abnormalities shown in electrocardiography and echocardiography .</p> <p><b>Comments:</b> It is a retrospective, multicenter cohort study, in which all included patients had been discharged or had died.</p>

**Ruan et al<sup>14</sup>** **Recovery:** Patients met the discharge criteria if they had no fever for at least 3 days, significantly improved respiratory function, and had negative SARS-CoV-2 laboratory test results twice in succession.

**Cardiovascular Disease:** No definition

**Myocardial Injury:** Median and interquartile range (IQR) values of cardiac troponin, pg/mL (2.0-28.0) were used.

**Comments:** It is a retrospective, dual-center cohort study, in which all included patients had been discharged or had died.

**Shi et al<sup>15</sup>** **Severe cases:** Patients who developed acute respiratory distress syndrome (ARDS). ARDS was defined according to the Berlin definition<sup>16</sup>.

**Recovery:** No definition.

**Cardiovascular Disease:** Patients who developed coronary heart disease and chronic heart disease. No definitions were provided.

**Myocardial Injury:** Blood levels of cardiac biomarkers (hs-TNI) above the 99th-percentile upper reference limit, regardless of new abnormalities in electrocardiography and echocardiography.

**Heart Failure:** No definition.

**Comments:** 319/416 (76.7) patients remained hospitalized at the time of the study.

**Guo et al**<sup>17</sup>

**Severe cases:** Patients who developed acute respiratory distress syndrome (ARDS). ARDS was defined according to the Berlin definition<sup>16</sup>.

**Recovery:** Successful treatment towards hospital discharge comprised relieved clinical symptoms, normal body temperature, significant resolution of inflammation as shown by chest radiography, and at least 2 consecutive negative results shown by real-time reverse transcription–polymerase chain reaction assay for COVID-19.

**Cardiovascular Disease:** Patients with coronary heart disease .

**Myocardial Injury:** Patients were considered to have acute myocardial injury if serum levels of troponin T (TnT) were above the 99th percentile upper reference limit.

**Arrhythmia:** Malignant arrhythmia was defined as rapid ventricular tachycardia lasting more than 30 seconds, inducing hemodynamic instability and/or ventricular fibrillation.

**Comments:** It is a retrospective, single-center cohort study, in which all included patients had been discharged or had died.

**Han et al**<sup>18</sup>

**Severe cases:** Severe cases met at least one of the following conditions: (a) shortness of breath, RR  $\geq$  30 times/min, (b) oxygen saturation (resting state)  $\leq$  93%, or (c) PaO<sub>2</sub>/FiO<sub>2</sub>  $\leq$  300mm Hg. Critical cases met at least one of the extra following conditions: (a) respiratory failure that needs to receive mechanical ventilation; (b) shock; and (c) multiple organ failure that need to be transferred to the intensive care unit (ICU).

**Recovery:** No definition.

**Myocardial Injury:** Patients were considered to have acute myocardial injury if cardiac troponin I (ultra-TnI) was above 0.04 ng/mL .

**Heart failure:** Patients were considered to have heart failure if N-terminal pro-brain natriuretic peptide (NT-proBNP) was above 900 pg/mL.

**Comments:** 3/273 (1.1) patients remained hospitalized at the time of the study.



**Chen et al**<sup>19</sup>

**Severe cases:** Patients who developed acute respiratory distress syndrome (ARDS). ARDS was defined according to the World Health Organization (WHO) interim guidance<sup>7</sup>.

**Recovery:** All the recovered patients with COVID-19 had completely resolved symptoms and signs, had significant improvement in pulmonary and extrapulmonary organ dysfunction, and no longer needed supportive care, with confirmed viral clearance by repeated tests for SARS-Cov-2 before hospital discharge.

**Cardiovascular Disease:** No definition.

**Myocardial Injury:** Serum levels of cardiac biomarkers (e.g. cardiac troponin I) were > the 99th percentile upper reference limit, or new abnormalities were shown in electrocardiography and echocardiography.

**Heart failure:** Using age-related amino-terminal pro-brain natriuretic peptide cut-points of 450, 900, and 1800 pg/mL for ages <50, 50-75, and >75, which yielded 90% sensitivity and 84% specificity for acute heart failure.

**Comments:** It is a retrospective, single-center cohort study, in which all included patients had been discharged or had died.

Arentz et al <sup>20</sup>	<p><b>Severe cases:</b> Critically ill patients. No definition of “critically ill” was provided.</p> <p><b>Recovery:</b> Patients who survived to be transferred out of ICU.</p> <p><b>Cardiovascular Disease:</b> Patients with chronic heart failure. No definition of chronic heart failure was provided.</p> <p><b>Myocardial Injury:</b> Patients with cardiomyopathy, which was defined as evidence of globally decreased left ventricular systolic function on transthoracic echocardiogram in addition to clinical signs of cardiogenic shock, an elevation in level of creatinine kinase or troponin I, or a decrease in central venous oxygen saturation (&lt;70%) without a past history of systolic dysfunction.</p> <p><b>Comments:</b> 8/21 (38.1) patients remained hospitalized at the time of the study.</p>
Mehra et al <sup>21</sup>	<p><b>Recovery:</b> Patients who survived to be discharged.</p> <p><b>Cardiovascular Disease:</b> Patients with coronary heart disease, congestive heart failure and arrhythmia. No definitions were provided.</p> <p><b>Comments:</b> The authors used an observational database from 169 hospitals in Asia, Europe, and North America. All included patients had been discharged or had died.</p>
Goyal et al <sup>22</sup>	<p><b>Severe cases:</b> Patients who received invasive mechanical ventilation.</p> <p><b>Cardiovascular Disease:</b> Patients with coronary heart disease.</p> <p><b>Arrhythmia:</b> Patients with atrial arrhythmias. No definition of atrial arrhythmias was provided</p> <p><b>Comments:</b> This retrospective case series includes adults with confirmed Covid-19 who were consecutively admitted in Manhattan. In total, 40 of the patients (10.2%) have died, and 260 (66.2%) have been discharged from the hospital; outcome data are incomplete for the remaining 93 patients (23.7%).</p>

<b>Lechien et al<sup>23</sup></b>	<p><b>Recovery:</b> Cured patients. No definition was provided.</p> <p><b>Cardiovascular Disease:</b> Patients with heart problems with no further explanation. No definition was provided</p> <p><b>Comments:</b> The authors recruited patients with positive diagnosis of Covid-19 from 18 European hospitals. Epidemiological and clinical data were obtained through a standardized questionnaire. Bayesian analysis was used for analyzing the relationship between outcomes.</p>
<b>Wei et al<sup>24</sup></b>	<p><b>Severe cases:</b> Severity of covid-19 was classified at the time of admission using the novel coronavirus pneumonia diagnostic criteria and treatment regimens defined by the National Health Commission of the People's Republic of China<sup>11</sup> and reclassified at the time of hospital discharge according to clinical evolution of the disease<sup>11</sup>.</p> <p><b>Cardiovascular Disease:</b> No definition.</p> <p><b>Myocardial Injury:</b> Acute myocardial injury was defined by a value of high-sensitivity troponin T greater 14pg/mL.</p>
<b>Richardson et al<sup>25</sup></b>	<p><b>Cardiovascular Disease:</b> Coronary heart disease and congestive heart failure. No definitions were provided.</p>
<b>Shi et al<sup>26</sup></b>	<p><b>Cardiovascular Disease:</b> Patients with coronary heart disease and chronic heart failure. No definitions were provided.</p> <p><b>Myocardial injury:</b> Myocardial injury was defined as blood levels of cardiac biomarkers cardiac troponin I increased above the 99th percentile upper reference limit.</p> <p><b>Heart failure:</b> Acute heart failure. No definition was provided.</p>

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COVID-19: Coronavirus disease 2019, CVD: cardiovascular disease, ICU: intensive care unit, SARS-Cov-2: Severe acute respiratory syndrome coronavirus 2

## References for Appendix

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